

EXHIBIT 1

Atch 19

1825B

HUMAN GENE TRANSFER PROTOCOLS

Updated Pr  
1986

8810-001<sup>a</sup> (M/TIL) Rosenberg, Steven A.; National Institutes of Health, Bethesda, Maryland; *The Treatment of Patients with Advanced Cancer Using Cyclophosphamide, Interleukin-2 and Tumor Infiltrating Lymphocytes.* RAC Approval: 10-3-88/NIH Approval: 3-2-89  
Minor Modification: 3-30-90

9007-002<sup>a,b</sup> (T/IGD/SCID-ADA) Blaese, R. Michael; National Institutes of Health, Bethesda, Maryland; *Treatment of Severe Combined Immune Deficiency (SCID) due to Adenosine Deaminase (ADA) Deficiency with Autologous Lymphocytes Transduced with the Human ADA Gene: An Experimental Study* RAC Approval: 7-31-90/NIH Approval: 9-6-90  
Major Amendment/RAC Approval: 2-10-92  
Major Amendment/NIH Approval: 4-22-92  
Minor Modification: 4-21-93  
Minor Modification: 6-7-93

9007-003<sup>a</sup> (T/C) Rosenberg, Steven A.; National Institutes of Health, Bethesda, Maryland; *Gene Therapy of Patients with Advanced Cancer Using Tumor Infiltrating Lymphocytes Transduced with the Gene Coding for Tumor Necrosis Factor.* RAC Approval: 7-31-90/NIH Approval: 9-6-90  
Minor Modification: 2-17-94

9102-004<sup>a</sup> (M/BM) Brenner, Malcolm K.; Mirro, Joseph; Hurwitz, Craig; Santana, Victor; and Ihle, James; St. Jude Children's Research Hospital, Memphis, Tennessee; *Autologous Bone Marrow Transplant for Children with Acute Myelogenous Leukemia in First Complete Remission: Use of Marker Genes to Investigate the Biology of Marrow Reconstitution and the Mechanism of Relapse.* RAC Approval: 2-4-91/NIH Approval: 7-12-91  
Minor Modification: 11-91  
CLOSED: 1-15-93

9105-005<sup>a</sup> (M/BM) Brenner, Malcolm K.; Mirro, Joseph; Santana, Victor; and Ihle, James; St. Jude Children's Research Hospital, Memphis, Tennessee; *A Phase I/II Trial of High Dose Carboplatin and Etoposide with Autologous Marrow Support for Treatment of Stage D Neuroblastoma in First Remission: Use of Marker Genes to Investigate the Biology of Marrow Reconstitution and the Mechanism of Relapse.* RAC Approval: 5-31-91/NIH Approval: 7-12-91  
Minor Modification: 11-91  
CLOSED: 6-1-92

9105-006<sup>a</sup> (M/BM) Brenner, Malcolm K.; Mirro, Joseph; Santana, Victor; and Ihle, James; St. Jude Children's Research Hospital, Memphis, Tennessee; *A Phase II Trial of High-Dose Carboplatin and Etoposide with Autologous Marrow Support for Treatment of Relapse/Refractory Neuroblastoma Without Apparent Bone Marrow Involvement.* RAC Approval: 5-31-91/NIH Approval: 7-12-91  
Minor Modification: 11-91  
CLOSED: 4-9-93

9105-007<sup>a</sup> (M/BM) Deisseroth, Albert B.; M.D. Anderson Cancer Research Center, Houston, Texas; *Autologous Bone Marrow Transplantation for Chronic Myelogenous Leukemia in which Retroviral Markers are Used to Discriminate between Relapse which Arises from Systemic Disease Remaining after Preparative Therapy Versus Relapse due to Residual Leukemic Cells in Autologous Marrow: A Pilot Trial.*  
 RAC Approval: 5-31-91/NIH Approval: 7-12-91  
 Minor Modification: 4-19-93  
 CLOSED: 6-1-93

9105-008 (M/H) Ledley, Fred D.; Woo, Savio; Ferry, George; and Hartwell, Whigennand; Baylor College of Medicine, Houston, Texas; *Hepatocellular Transplantation in Acute Hepatic Failure and Targeting Genetic Markers to Hepatic Cells.*  
 RAC Approval: 5-30-91/NIH Approval: 7-12-91  
 CLOSED: Protocol Never Initiated

9105-009<sup>a</sup> (M/TIL) Lotze, Michael T.; University of Pittsburgh School of Medicine, Pittsburgh, Pennsylvania; *The Administration of Interleukin-2 and Tumor Infiltrating Lymphocytes to Patients with Melanoma.*  
 RAC Approval: 5-30-91/NIH Approval: 1-17-92  
 Minor Modification: 11-30-92

9110-010<sup>a</sup> (T/V/C) Rosenberg, Steven A.; National Institutes of Health, Bethesda, Maryland; *Immunization of Cancer Patients Using Autologous Cancer Cells Modified by Insertion of the Gene for Tumor Necrosis Factor (TNF).*  
 RAC Approval: 10-7-91/NIH Approval: 10-15-91  
 Minor Modification: 7-9-92

9110-011 (T/V/C) Rosenberg, Steven A.; National Institutes of Health, Bethesda, Maryland; *Immunization of Cancer Patients Using Autologous Cancer Cells Modified by Insertion of the Gene for Interleukin-2 (IL-2).*  
 RAC Approval: 10-7-91/NIH Approval: 10-15-91

9110-012<sup>a</sup> (T/IGD/Familial Hypercholesterolemia) Wilson, James M.; University of Pennsylvania Medical Center, Philadelphia, Pennsylvania; *Ex Vivo Gene Therapy of Familial Hypercholesterolemia.*  
 RAC Approval: 10-8-91/NIH Approval: 11-14-91  
 Minor Modification: 12-3-92  
 Minor Modification: 8-18-93  
 CLOSED: 3-11-94

9202-013<sup>a</sup> (T/C) Nabel, Gary J.; University of Michigan, Ann Arbor, Michigan; *Immunotherapy of Malignancy by In Vivo Gene Transfer into Tumors.*  
 RAC Approval: 2-10-92/NIH Approval: 4-17-92  
 Minor Modification: 1-22-93  
 Minor Modification: 1-93  
 CLOSED: 11-19-92

9202-014 (M/BM) Cornetta, Kenneth; Indiana University, Indianapolis, Indiana; *Retroviral-Mediated Gene Transfer of Bone Marrow Cells during Autologous Bone Marrow Transplantation for Acute Leukemia.*  
 RAC Approval: 2-11-92/NIH Approval: 4-17-92

9202-015

(M/PB/TIL)

Economou, James S. and Belldegrun, Arie; University of California at Los Angeles, Los Angeles, California; *The Treatment of Patients with Metastatic Melanoma and Renal Cell Cancer Using In Vitro Expanded and Genetically-Engineered (Neomycin Phosphotransferase) Bulk, CD8 (+) and/or CD4(+) Tumor Infiltrating Lymphocytes and Bulk, CD8(+) and/or CD4(+) Peripheral Blood Leukocytes in Combination with Recombinant Interleukin-2 Alone, or with Recombinant Interleukin-2 and Recombinant Alpha Interferon.*

RAC Approval: 2-11-92/NIH Approval: 4-17-92

CLOSED: 6-94

9202-016<sup>a</sup>

(T/V/C/Ovarian)

Freeman, Scott M.; Tulane University Medical Center, New Orleans, Louisiana; *Gene Transfer for the Treatment of Cancer.*

RAC Approval: 2-10-92/NIH Approval: 2-5-93

Minor Modification: 8-6-93

9202-017<sup>b</sup>

(M/CTL)

Greenberg, Philip D. and Riddell, Stanley; Fred Hutchinson Cancer Research Center, University of Washington, Seattle; *Phase I Study to Evaluate the Safety of Cellular Adoptive Immunotherapy using Genetically Modified CD8+ HIV-Specific T Cells in HIV Seropositive Individuals.*

RAC Approval: 2-11-92/NIH Approval: 4-17-92

Major Amendment/RAC Approval: 9-9-93

Major Amendment/NIH Approval: 10-7-93

9206-018<sup>a</sup>

(T/V/C/Neuroblastoma)

Brenner, Malcolm K.; Furman, Wayne; Santana, Victor; Bowman, Laura; and Meyer, William; St. Jude Children's Research Hospital, Memphis, Tennessee; *Phase I Study of Cytokine-Gene Modified Autologous Neuroblastoma Cells for Treatment of Relapsed/Refractory Neuroblastoma.*

RAC Approval: 6-1-92/NIH Approval: 8-14-92

Minor Modification: 6-23-94

9206-019<sup>a</sup>

(T/C/Brain)

Oldfield, Edward; National Institutes of Health, Bethesda, Maryland; *Gene Therapy for the Treatment of Brain Tumors Using Intra-Tumoral Transduction with the Thymidine Kinase Gene and Intravenous Ganciclovir.*

RAC Approval: 6-1-92/NIH Approval: 8-14-92

Minor Modification: 11-29-93

9206-020<sup>a</sup>

(M/BM/PB)

Deisseroth, Albert B.; MD Anderson Cancer Center, Houston, Texas; *Use of Two Retroviral Markers to Test Relative Contribution of Marrow and Peripheral Blood Autologous Cells to Recovery After Preparative Therapy.*

RAC Approval: 6-2-92/NIH Approval: 8-14-92

Minor Modification: 4-19-93

9206-021

(T/V/C/Melanoma)

Gansbacher, Bernd; Houghton, Alan; and Livingston, Philip; Memorial Sloan Kettering Cancer Center, New York, New York; *Immunization with HLA-A2 matched Allogeneic Melanoma Cell Secrete Interleukin-2 in Patients with Metastatic Melanoma.*

RAC Approval: 6-2-92/NIH Approval: 8-14-92

CLOSED: 10-19-94

9206-022<sup>a</sup> (T/V/C/Renal Cell)  
Gansbacher, Bernd; Motzer, Robert; Houghton, Alan; and Bander, Neil; Memorial Sloan Kettering Cancer Center, New York, New York; *Immunization with Interleukin-2 Secreting Allogeneic HLA-A2 Matched Renal Cell Carcinoma Cells in Patients with Advanced Renal Cell Carcinoma.*  
RAC Approval: 6-2-92/NIH Approval: 8-14-92  
Minor Modification: 3-31-93

9206-023<sup>a</sup> (M/BM/PB)  
Dunbar, Cynthia; National Institutes of Health, Bethesda, Maryland; *Retroviral-Mediated Gene Transfer of Bone Marrow and Peripheral Blood Stem Cells During Autologous Bone Marrow Transplantation for Multiple Myeloma.*  
RAC Approval: 6-2-92/NIH Approval: 8-14-92  
Minor Modification: 1-6-94  
Minor Modification: 3-23-94

9206-024<sup>a</sup> (M/BM/PB)  
Dunbar, Cynthia; National Institutes of Health, Bethesda, Maryland; *Retroviral-Mediated Gene Transfer of Bone Marrow and Peripheral Blood Stem Cells During Autologous Bone Marrow Transplantation for Metastatic Breast Cancer.*  
RAC Approval: 6-2-92/NIH Approval: 8-14-92  
Minor Modification: 1-6-94

9206-025<sup>a</sup> (M/BM/PB)  
Dunbar, Cynthia; National Institutes of Health, Bethesda, Maryland; *Retroviral-Mediated Gene Transfer of Bone Marrow and Peripheral Blood Stem Cells During Autologous Bone Marrow Transplantation for Chronic Myelogenous Leukemia.*  
RAC Approval: 6-2-92/NIH Approval: 8-14-92  
Minor Modification: 1-6-94  
Minor Modification: 3-23-94

9209-026<sup>a</sup> (M/PB)  
Walker, Robert E.; National Institutes of Health, Bethesda, Maryland; *A Study of the Safety and Survival of the Adoptive Transfer of Genetically Marked Syngeneic Lymphocytes in HIV Infected Identical Twins.*  
RAC Approval: 9-14-92/NIH Approval: 9-3-93  
Minor Modification: 6-1-94

9209-027<sup>a</sup> (M/PB)  
Schuening, Friedrich G.; Fred Hutchinson Cancer Research Center, University of Washington, Seattle, Washington; *A Phase I/II Study of PIXY321, a rhGM-CSF/rhIL-3 Fusion Protein or rhG-CSF, for the Mobilization of Peripheral Blood Stem Cells for Autologous Stem Cell Transplantation.*  
RAC Approval: 9-14-92/NIH Approval: 2-5-93  
Minor Modification: 2-25-94

9209-028<sup>a</sup> (M/PBSC)  
Schuening, Friedrich G.; Fred Hutchinson Cancer Research Center, University of Washington, Seattle, Washington; *Evaluation of the Use of Recombinant Human G-CSF Stimulated Peripheral Blood Progenitor Cell Supplementation in Autologous Bone Marrow Transplantation in Patients with Lymphoid Malignancies.*  
RAC Approval: 9-14-92/NIH Approval: 2-5-93  
Minor Modification 2-25-94  
CLOSED: 2-25-94 (Merged with protocol # 9209-027)

9209-029

(M/BM/PB)

Schuening, Friedrich G.; Fred Hutchinson Cancer Research Center, University of Washington, Seattle, Washington; *A Trial of G-CSF Stimulated Peripheral Blood Stem Cells for Engraftment in Identical Twins.*

RAC Approval: 9-14-92/NIH Approval: 2-5-93

CLOSED: Protocol Never Initiated

9209-030<sup>a</sup>

(M/BM/PB)

Deisseroth, Albert B.; University of Texas MD Anderson Cancer Center, Houston, Texas; *Use of Retroviral Markers to Identify Efficacy of Purging and Origin of Relapse Following Autologous Bone Marrow and Peripheral Blood Cell Transplantation in Indolent B Cell Neoplasms (Follicular Non-Hodgkin's Lymphoma or Chronic Lymphocytic Leukemia) Patients.*

RAC Approval: 9-14-92/NIH Approval: 12-2-93

Minor Modification: 11-3-93

Minor Modification: 11-18-93

Minor Modification: 10-27-94

9403-031

(T/C/Non-small Cell Lung Cancer)

Roth, Jack A.; The University of Texas MD Anderson Cancer Center, Houston, Texas; *Clinical Protocol for Modification of Oncogene and Tumor Suppressor Gene Expression in Non-Small Cell Lung Cancer NSCLC.*

9209-031/ RAC Approval of Original Protocol: 9-15-92/

RAC Approval of Original Protocol Withdrawn 12-3-93

9403-031/ RAC Approval of Resubmitted Protocol: 3-4-94/

NIH Approval of Resubmitted Protocol: 1-4-95

9209-032

(M/BM)

Brenner, Malcolm K.; St. Jude Children's Research Hospital, Memphis, Tennessee; *A Phase II Trial of the Baxter Neuroblastoma Bone Marrow Purging System Using Gene Marking to Assess Efficacy.*

RAC Approval: 9-15-92/NIH Approval: 2-5-93

9209-033

(T/V/C)

Lotze, Michael T. and Rubin, Joshua T.; University of Pittsburgh, Pittsburgh, Pennsylvania; *Gene Therapy of Cancer: A Pilot Study of IL-4 Gene Modified Antitumor Vaccines.*

RAC Approval: 9-15-92/NIH Approval: 2-5-93

9212-034<sup>a</sup>

(T/IGD/Cystic Fibrosis)

Crystal, Ronald G.; New York Hospital-Cornell Medical Center; *A Phase I Study, in Cystic Fibrosis Patients, of the Safety, Toxicity, and Biological Efficacy of a Single Administration of a Replication Deficient, Recombinant Adenovirus Carrying the cDNA of the Normal Human Cystic Fibrosis Transmembrane Conductance Regulator Gene in the Lung.*

RAC Approval: 12-3-92/NIH Approval: 4-16-93

Minor Modification: 5-17-93

Minor Modification: 10-8-93

Minor Modification: 11-29-93

Minor Modification: 2-4-94

Minor Modification: 12-8-94

9212-035<sup>a</sup>

(T/IGD/Cystic Fibrosis)

Wilson, James M.; University of Pennsylvania Medical Center, Philadelphia, Pennsylvania, and Richard H. Simon; University of Michigan Medical Center, Ann Arbor, Michigan; *Gene Therapy of Cystic Fibrosis Lung Diseases Using E1 Deleted Adenoviruses: A Phase I Trial.*  
RAC Approval: 12-3-92/NIH Approval: 8-26-93

Minor Modification: 8-17-93

Minor Modification: 8-26-93

Minor Modification: 8-31-94

9212-036<sup>a</sup>

(T/IGD/Cystic Fibrosis)

Welsh, Michael J.; Howard Hughes Medical Institute, Iowa City, Iowa, and Smith, Alan E.; Genzyme Corporation, Framingham, Massachusetts; *Cystic Fibrosis Gene Therapy Using an Adenovirus Vector: In Vivo Safety and Efficacy in Nasal Epithelium.*  
RAC Approval: 12-4-92/NIH Approval: 4-16-93

Minor Modification: 10-18-93

9303-037<sup>a</sup>

(T/C/Glioblastoma Multiforme)

Van Gilder, John C.; University of Iowa, Iowa City, Iowa, Berger, Mitchel; University of California, San Francisco, California, and Prados, Michael; University of Washington, Seattle, Washington; *Gene Therapy for the Treatment of Recurrent Glioblastoma Multiforme with In Vivo Tumor Transduction with the Herpes Simplex Thymidine Kinase Gene/Ganciclovir System.*  
RAC Approval: 3-1-93/NIH Approval: 4-16-93

Minor Modification: 7-13-94

Minor Modification: 11-30-94

9303-038

(M/EBV-CTL)

Heslop, Helen E.; Brenner, Malcolm K.; and Rooney, Cliona; St. Jude Children's Research Hospital, Memphis, Tennessee; *Administration of Neomycin Resistance Gene Marked EBV Specific Cytotoxic T Lymphocytes to Recipients of Mismatched-Related or Phenotypically Similar Unrelated Donor Marrow Grafts.* RAC Approval: 3-2-93/NIH Approval: 4-16-93  
Minor Modification: 8-31-94

9303-039

(M/BM)

Brenner, Malcolm K.; Krance, Robert; Heslop, Helen E.; Santana, Victor; and Ihle, James; St. Jude Children's Research Hospital, Memphis, Tennessee; *Assessment of the Efficacy of Purging by Using Gene-Marked Autologous Marrow Transplantation for Children with Acute Myelogenous Leukemia in First Complete Remission.*

RAC Approval: 3-2-93/NIH Approval: 4-16-93

9303-040

(T/V/C/Renal Cell)

Simons, Jonathan; Johns Hopkins Oncology Center, Baltimore, Maryland; *Phase I Study of Non-Replicating Autologous Tumor Cell Injections Using Cells Prepared With or Without Granulocyte-Macrophage Colony Stimulating Factor Gene Transduction in Patients with Metastatic Renal Cell Carcinoma.*

RAC Approval: 3-1-93/NIH Approval: 12-2-93

9303-041<sup>a</sup>

(T/IGD/Cystic Fibrosis)

Wilmott, Robert W. and Whitsett, Jeffrey, Children's Hospital Medical Center, Cincinnati, Ohio, and Trapnell, Bruce; Genetic Therapy, Inc., Gaithersburg, Maryland; *A Phase I Study of Gene Therapy of Cystic Fibrosis Utilizing a Replication Deficient Recombinant Adenovirus Vector to Deliver the Human Cystic Fibrosis Transmembrane Conductance Regulator cDNA to the Airways.*  
RAC Approval: 3-2-93/NIH Approval: 4-16-93

Minor Modification: 4-13-94

Minor Modification: 8-31-94

9303-042<sup>a</sup>

(T/IGD/Cystic Fibrosis)

Boucher, Richard C. and Knowles, Michael R.; University of North Carolina, Chapel Hill, North Carolina; *Gene Therapy for Cystic Fibrosis Using E1 Deleted Adenovirus: A Phase I Trial in the Airway Cavity.*

RAC Approval: 3-2-93/NIH Approval: 10-7-93

Minor Modification: 2-17-94

Minor Modification: 9-30-94

CLOSED: 10-94

9306-043<sup>a</sup>

(T/V/C/Melanoma)

Seigler, Hilliard F.; Duke University Medical Center, Durham, North Carolina; and Merritt, Jame A.; Viagene, Inc., San Diego, California; *A Phase I Trial of Human Gamma Interferon-Transduced Autologous Tumor Cells in Patients With Disseminated Malignant Melanoma.*

RAC Approval: 6-7-93/NIH Approval: 9-3-93

Minor Modification: 7-11-94

Minor Modification: 10-12-94

9306-044<sup>a</sup>

(T/C/Ovarian)

Deisseroth, Albert B.; Kavanagh, John; and Champlin, Richard; University of Texas MD Anderson Cancer Center, Houston, Texas; *Use of Safety-Modified Retroviruses to Introduce Chemotherapy Resistance Sequences into Normal Hematopoietic Cells for Chemoprotection During the Therapy of Ovarian Cancer: A Pilot Trial.*

RAC Approval: 6-7-93/NIH Approval: 12-2-93

Minor Modification: 2-25-94

Minor Modification: 2-25-94

9306-045<sup>a</sup>

(T/C)

Nabel, Gary J.; University of Michigan Medical Center, Ann Arbor, Michigan; *Immunotherapy for Cancer by Direct Gene Transfer into Tumors.*

RAC Approval: 6-7-93/NIH Approval: 9-3-93

Minor Modification: 11-21-94

9306-046

(T/IGD/Gaucher Disease)

Barranger, John A.; University of Pittsburgh, Pittsburgh, Pennsylvania, *Gene Therapy for Gaucher Disease: Ex Vivo Gene Transfer and Autologous Transplantation of CD34(+) Cells.*

RAC Approval: 6-7-93/NIH Approval: 9-3-93

9306-047

(T/IGD/Gaucher Disease)

Karlsson, Stefan and Dunbar, Cynthia; National Institutes of Health, Bethesda, Maryland, and Kohn Donald B.; Childrens Hospital Los Angeles, Los Angeles, California; *Retroviral Mediated Transfer of the cDNA for Human Glucocerebrosidase into Hematopoietic Stem Cells of Patients with Gaucher Disease.*

RAC Approval: 6-7-93/NIH Approval: 9-3-93

9306-048<sup>a</sup>

(T/HIV)

Galpin, Jeffrey E.; University of Southern California, Casciato, Dennis A.; Shared Medical Research Foundation, Tarzana, California, and Merritt, James A.; Viagene, Inc., San Diego, California; *A Preliminary Study to Evaluate the Safety and Biologic Effects of Murine Retroviral Vector Encoding HIV-1 Genes [HIV-1(V)] in Asymptomatic Subjects Infected with HIV-1.*

RAC Approval: 6-7-93/NIH Approval: 9-3-93

Minor Modification: 7-11-94

Minor Modification: 10-12-94

CLOSED: 9-8-94

9306-049 (T/HIV) Nabel, Gary J.; University of Michigan Medical Center, Ann Arbor, Michigan; *A Molecular Genetic Intervention for AIDS - Effects of a Transdominant Negative Form of Rev.* RAC Approval: 6-7-93/NIH Approval: 9-3-93

9306-EXP (T/V/C/Glioblastoma) Sobol, Robert and Royston, Ivor; San Diego Regional Cancer Center, San Diego, California; *Phase I Study of Cytokine Gene Therapy of Cancer. Active Immunotherapy of Glioblastoma with Tumor Cells or Fibroblasts Genetically Modified to Secrete Interleukin-2.* NIH Approval: 12-28-92 Major Amendment (Expedited Review)/NIH Approval: 5-11-93 CLOSED: 10-20-93 (Patient death)

9306-050 (T/C/Astrocytoma) Raffel, Corey; Childrens Hospital Los Angeles, Los Angeles, California, and Culver, Kenneth; Iowa Methodist Medical Center, Des Moines, Iowa; *Gene Therapy for the Treatment of Recurrent Pediatric Malignant Astrocytomas with In Vivo Tumor Transduction with the Herpes Simplex Thymidine Kinase Gene.* RAC Approval: 6-8-93/NIH Approval: 9-3-93

9306-051 (T/C/Breast/Ovarian/Brain) Hesdorffer, Charles and Antman, Karen; Columbia University College of Physicians and Surgeons, New York, New York; *Human MDR Gene Transfer in Patients with Advanced Cancer.* RAC Approval: 6-8-93/NIH Approval: 9-3-93

9306-052 (T/V/C/Glioblastoma) Ilan, Joseph; Case Western Reserve University School of Medicine and University Hospitals of Cleveland, Cleveland, Ohio; *Gene Therapy for Human Brain Tumors Using Episome-Based Antisense cDNA Transcription of Insulin-Like Growth Factor I.* RAC Approval: 6-8-93/NIH Approval: 12-2-93

9309-053<sup>a</sup> (T/V/C/Small Cell Lung Cancer) Cassileth, Peter; Podack, Eckhard R.; Sridhar, Kasi; University of Miami, and Savaraj, Niramol; Miami Veterans Administration Hospital, Miami, Florida; *Phase I Study of Transfected Cancer Cells Expressing the Interleukin-2 Gene Product in Limited Stage Small Cell Lung Cancer.* RAC Approval: 9-9-93/NIH Approval: 12-2-93 Minor Modification: 3-23-94

9309-054 (T/C/Breast) O'Shaughnessy, Joyce; National Institutes of Health, Bethesda, Maryland; *Retroviral Mediated Transfer of the Human Multi-Drug Resistance Gene (MDR-1) into Hematopoietic Stem Cells During Autologous Transplantation after Intensive Chemotherapy for Breast Cancer.* RAC Approval: 9-9-93/NIH Approval: 10-7-93

9309-055 (T/C/Brain) Kun, Larry E.; Sanford, R. A.; Brenner, Malcolm K.; and Heideman, Richard L.; St. Jude Childrens Research Hospital, Memphis, Tennessee; and Oldfield, Edward H.; National Institutes of Health, Bethesda, Maryland; *Gene Therapy for Recurrent Pediatric Brain Tumors.* RAC Approval: 9-9-93/NIH Approval: 10-7-93

9309-056 (T/V/C/Melanoma) Das Gupta, Tapas K. and Cohen, Edward P.; University of Illinois at Chicago; Chicago, Illinois; *Immunization of Malignant Melanoma Patients with Interleukin 2-Secreting Melanoma Cells Expressing Defined Allogeneic Histocompatibility Antigens.* RAC Approval: 9-10-93/NIH Approval: 4-19-94

9309-057 (T/HIV) Wong-Staal, Flossie; Poeschla, Eric; and Looney, David; University of California, San Diego, California; *A Phase I Clinical Trial to Evaluate the Safety and Effects in HIV-1 Infected Humans Autologous Lymphocytes Transduced with a Ribozyme that Cleaves HIV-1 RNA.* RAC Approval: 9-10-93/NIH Approval: 10-25-94

9309-058 (T/V/C/Melanoma) Economou, James S. and Glasby, John A.; University of California Medical Center, Los Angeles, California; *Genetically Engineered Autologous Tumor Vaccines Producing Interleukin-2 for the Treatment of Metastatic Melanoma.* RAC Approval: 9-10-93/NIH Approval: 12-2-93

9312-059<sup>a</sup> (T/C/Leptomeningeal Carcinomatosis) Oldfield, Edward H. and Ram, Zvi; NIH, Bethesda, Maryland; *Intrathecal Gene Therapy for the Treatment of Leptomeningeal Carcinomatosis.* RAC Approval: 12-2-93/NIH Approval: 1-20-94 Minor Modification: 7-5-94

9312-060<sup>a</sup> (T/V/C) Sobol, Robert E. and Royston, Ivor; San Diego Regional Cancer Center, San Diego, California; *Injection of Colon Carcinoma Patients with Autologous Irradiated Tumor Cells and Fibroblasts Genetically Modified to Secrete Interleukin-2.* RAC Approval: 12-2-93/NIH Approval: 1-4-95 Minor Modification: 1-24-95

9312-061 (T/IGD/Gaucher Disease) Schuening, Friedrich; Fred Hutchinson Cancer Research Center, Seattle, Washington; *Retrovirus-Mediated Transfer of the cDNA for Human Glucocerebrosidase into Peripheral Blood Repopulating Cells of Patients with Gaucher's Disease.* RAC Approval: 12-2-93/NIH Approval: 11-15-94

9312-062<sup>a</sup> (T/HIV) Haubrich, Richard; University of California at San Diego Treatment Center, San Diego, California, and Merritt, James A.; Viagene, Inc., San Diego, California; *An Open Label, Phase I/II Clinical Trial to Evaluate the Safety and Biological Activity of HIV-IT(V) (HIV-1 IIBenv/Retroviral Vector) in HIV-1 Infected Subjects.* RAC Approval: 12-3-93/NIH Approval: 4-19-94 Minor Modification: 7-11-94 Minor Modification: 10-12-94 CLOSED: 10-13-94

9312-063 (T/V/C/Melanoma) Sznol, Mario; National Institutes of Health, Frederick, Maryland; *A Phase I Trial of B7-Transfected Lethally Irradiated Allogeneic Melanoma Cell Lines to Induce Cell Mediated Immunity Against Tumor Associated Antigens Presented by HLA-A2 or HLA-A1 in Patients with Stage IV Melanoma.* RAC Approval: 12-3-93/NIH Approval: 4-19-94

9312-064 (T/C/Colorectal) Rubin, Joseph; Mayo Clinic, Rochester, Minnesota; *Phase I Study of Immunotherapy of Advanced Colorectal Carcinoma by Direct Gene Transfer into Hepatic Metastases.* RAC Approval: 12-3-93/NIH Approval: 4-19-94

9312-065 (T/V/C/Melanoma)  
Chang, Alfred E.; University of Michigan, Ann Arbor, Michigan; *Adoptive Immunotherapy of Melanoma with Activated Lymph Node Cells Primed In Vivo with Autologous Tumor Cells Transduced with the IL-4 Gene.*  
RAC Approval: 12-3-93/NIH Approval: 8-23-94

9312-066 (T/IGD/Cystic Fibrosis)  
Sorscher, Eric J. and Logan, James L.; University of Alabama, Birmingham, Alabama; *Gene Therapy for Cystic Fibrosis Using Cationic Liposome Mediated Gene Transfer. A Phase I Trial of Safety and Efficacy in the Nasal Airway.*  
RAC Approval: 12-3-93/NIH Approval: 1-4-95

9312-067<sup>a</sup> (T/IGD/Cystic Fibrosis)  
Welsh, Michael J.; Howard Hughes Medical Institute, Iowa City, Iowa; *Adenovirus-Mediated Gene Transfer of CFTR to the Nasal Epithelium and Maxillary Sinus of Patients with Cystic Fibrosis.*  
RAC Approval: 12-3-93/NIH Approval: 2-10-94  
Minor Modification: 2-17-94

9403-068<sup>a</sup> (T/V/C/Neuroblastoma)  
Rosenblatt, Joseph; University of California, Los Angeles, California; Seeger, Robert, Childrens Hospital, Los Angeles, California, and Merritt, James A.; Viagene, Inc., San Diego, California; *A Phase I Study of Immunization with Gamma Interferon Transduced Neuroblastoma Cells.*  
RAC Approval: 3-3-94/NIH Approval: 10-25-94  
Minor Modification: 7-11-94  
Minor Modification: 10-12-94

9403-069 (T/HIV)  
Walker, Robert; NIH, Bethesda, Maryland; *A Phase I/II Pilot Study of the Safety of the Adoptive Transfer of Syngeneic Gene-Modified Cytotoxic T-Lymphocytes in HIV-Infected Identical Twins.*  
RAC Approval: 3-3-94/NIH Approval: 8-23-94

9403-070 (T/IGD/Alpha-1-Antitrypsin Deficiency)  
Brigham, Kenneth; Vanderbilt University, Nashville, Tennessee; *Expression of an Exogenously Administered Human Alpha-1-Antitrypsin Gene in the Respiratory Tract of Humans.*  
RAC Approval: 3-3-94/NIH Approval: 10-25-94

9403-071 (T/C/Renal Cell)  
Vogelzang, Nicholas; the University of Chicago, Chicago, Illinois; *Phase I Study of Immunotherapy for Metastatic Renal Cell Carcinoma by Direct Gene Transfer into Metastatic Lesions.*  
RAC Approval: 3-4-94/NIH Approval: 4-19-94

9403-072<sup>a</sup> (T/C/Melanoma)  
Hersh, Evan; Arizona Cancer Center, Tuscon, Arizona; and Akporiaye, Harris; Stopeck; Unger; and Warneke; the University of Arizona, Tuscon, Arizona; *Phase I Study of Immunotherapy of Malignant Melanoma by Direct Gene Transfer.*  
RAC Approval: 3-4-94/NIH Approval: 4-19-94  
Minor Modification: 11-30-94

9406-073 (T/C/Colorectal)  
Curiel, David; University of Alabama, Birmingham, Alabama; *Phase I Trial of a Polynucleotide Augmented Anti-tumor Immunization to Human Carcinoembryonic Antigen in Patients with Metastatic Colorectal Cancer.*  
RAC Approval: 6-9-94/NIH Approval: Disapproved

9406-074 (T/O/Rheumatoid Arthritis)  
Evans, C. H. and Robbins, Paul; University of Pittsburgh, Pittsburgh, Pennsylvania; Clinical Trial to Assess the Safety, Feasibility, and Efficacy of Transferring a Potentially Anti-arthritis Cytokine Gene Human Joints with Rheumatoid Arthritis.  
RAC Approval: 6-9-94/NIH Approval: Pending

9406-075 (M/PB/TIL)  
Freedman, Ralph; MD Anderson Cancer Center, Houston, Texas; Use of a Retroviral Vector to Study the Trafficking Patterns of Purified Ovarian TIL Populations Used in Intraperitoneal Adoptive Immunotherapy of Ovarian Cancer Patients: A Pilot Study.  
RAC Approval: 6-9-94/NIH Approval: 7-12-94

9406-076 ((M/PBSC)  
Heslop, Helen; Brenner, Malcolm, K.; and Krance, Robert; St. Jude Childrens Research Hospital, Memphis, Tennessee; Use of Double Marking with Retroviral Vectors to Determine the Rate of Reconstitution of Untreated and Cytokine Expanded CD34(+) Selected Marrow Cells in Patients Undergoing Autologous Bone Marrow Transplantation.  
RAC Approval: 6-9-94/NIH Approval: 7-12-94

9406-077 (T/C/Breast)  
Deisseroth, Albert; Hortobagyi, Gabriel; Champlin, Richard; and Holmes, Frankie; MD Anderson Cancer Center, Houston, Texas; Use of Safety-Modified Retroviruses to Introduce Chemotherapy Resistance Sequences into Normal Hematopoietic Cells for Chemoprotection During the Therapy of Breast Cancer: A Pilot Trial.  
RAC Approval: 6-9-94/NIH Approval: 7-12-94

9406-078 (T/IGD/Fanconi Anemia)  
Liu, Johnson, M. and Young, Neal S.; National Institutes of Health, Bethesda, Maryland; Retroviral Mediated Gene Transfer of the Fanconi Anemia Complementation Group C Gene to Hematopoietic Progenitors of Group C Patients.  
RAC Approval: 6-9-94/NIH Approval: 2-12-94

9406-079 (T/C/Non-smal Cell Lung Cancer)  
Roth, Jack A.; MD Anderson Cancer Center, Houston, Texas; Clinical Protocol for Modification of Tumor Suppressor Gene Expression and Induction of Apoptosis in Non-Small Cell Lung Cancer (NSCLC) with an Adenovirus Vector Expressing Wildtype p53 and Cisplatin.  
RAC Approval: 6-10-94/NIH Approval: Pending

9406-080 (T/V/C/Glioblastoma)  
Sobol, Robert and Royston, Ivor; San Diego Regional Cancer Center, San Diego, California; Injection of Glioblastoma Patients with Tumor Cells Genetically Modified to Secrete Interleukin-2 (IL-2): A Phase I Study.  
RAC Approval: 6-10-94/NIH Approval: 7-12-94

9406-081 (T/V/C/Melanoma/T Cell Lymphoma/Breast/Head and Neck)  
Lotze, Michael T; University of Pittsburgh, Pittsburgh, Pennsylvania; IL-12 Gene Therapy Using Direct Injection of Tumor with Genetically Engineered Autologous Fibroblasts.  
RAC Approval: 6-10-94/NIH Approval: 2-10-95

9408-082 (T/V/C/Prostate)  
Simons, Jonathan; Johns Hopkins Oncology Center, Baltimore, Maryland; Phase I/II Study of Autologous Human GM-CSF Gene Transduced Prostate Cancer Vaccines in Patients with Metastatic Prostate Carcinoma.  
NIH/ORDA Approval: 8-3-94 (Accelerated Review)

9409-083 (T/IGD/Cystic Fibrosis)  
 Flotte, Terence R.; Johns Hopkins Childrens Center, Baltimore, Maryland; *A Phase I Study of an Adeno-associated Virus-CFTR Gene Vector in Adult CF Patients with Mild Lung Disease.*  
 RAC Approval: 9-12-94/NIH Approval: 11-15-94

9409-084 (T/C/Breast)  
 Holt, Jeffrey, and Arteaga, Carlos B.; Vanderbilt University, Nashville, Tennessee; *Gene Therapy for the Treatment of Metastatic Breast Cancer by In Vivo Infection with Breast-Targeted Retroviral Vectors Expressing Antisense c-fos or Antisense c-myc RNA.*  
 RAC Approval: 9-12-94/NIH Approval: 1-4-95

9409-085<sup>a</sup> (T/IGD/Cystic Fibrosis)  
 Crystal, Ronald G.; New York Hospital-Cornell Medical Center, New York, New York; *Evaluation of Repeat Administration of a Replication Deficient, Recombinant Adenovirus Containing the Normal Cystic Fibrosis Transmembrane Conductance Regulator cDNA to the Airways of Individuals with Cystic Fibrosis.*  
 RAC Approval: 9-12-94/NIH Approval: 11-30-94  
 Minor Modification: 11-3-94

9409-086 (T/V/C/Breast)  
 Lyerly, H. Kim; Duke University Medical Center, Durham, North Carolina; *A Pilot Study of Autologous Human Interleukin-2 Gene Modified Tumor Cells in Patients with Refractory or Recurrent Metastatic Breast Cancer.*  
 RAC Approval: 9-12-94/NIH Approval: 10-25-94

9409-087 (T/IGD/Hunter Syndrome)  
Whitley, Chester B.; University of Minnesota, Minneapolis, Minnesota; Retroviral-Mediated Transfer of the Iduronate-2-Sulfatase Gene into Lymphocytes for Treatment of Mild Hunter Syndrome (Mucopolysaccharidosis Type II).  
RAC Approval: 9-13-94/NIH Approval: Pending

9409-088 (T/O/Peripheral Artery Disease)  
 Isner, Jeffrey M. and Walsh, Kenneth; St. Elizabeth's Medical Center, Tufts University, Boston, Massachusetts; *Arterial Gene Transfer for Therapeutic Angiogenesis in Patients with Peripheral Artery Disease.*  
 RAC Approval: 9-13-94/NIH Approval: 11-15-94

9409-089 (T/C/Malignant Glioma)  
Eck, Stephen L. and Alavi, Jane B.; University of Pennsylvania Medical Center, Philadelphia, Pennsylvania; Treatment of Advanced CNS Malignancy with the Recombinant Adenovirus H5.020RSVTK: A Phase I Trial.  
RAC Approval: 9-13-94/NIH Approval: Pending

9409-090 (T/C/Malignant Mesothelioma)  
 Albelda, Steven M.; University of Pennsylvania Medical Center, Philadelphia, Pennsylvania; *Treatment of Advanced Mesothelioma with the Recombinant Adenovirus H5.010RSVTK: A Phase I Trial.*  
 RAC Approval: 9-13-94/NIH Approval: 1-4-95

9409-091 (T/IGD/Cystic Fibrosis)  
 Dorkin, Henry L.; New England Medical Center, Tufts University, Boston, Massachusetts; and Lapey, Allen; Massachusetts General Hospital, Harvard Medical School, Boston, Massachusetts; *Adenovirus Mediated Gene Transfer for Cystic Fibrosis: Safety of Single Administration in the Lung (lobar instillation).*  
 NIH/ORDA Approval: 10-5-94 (Accelerated Review)

9411-092

(M/BMSC/PBSC)

Douer, Dan; University of Southern California, Kenneth Norris Jr. Comprehensive Cancer Center and Hospital, Los Angeles, California; *High Dose Chemotherapy and Autologous Bone Marrow and Peripheral Blood Stem Cell Transplantation for Patients with Lymphoma or Metastatic Breast Cancer: Use of Marker Genes to Investigate the Biology of Hematopoietic Reconstitution in Adults.*  
NIH/ORDA Approval: 11-18-94 (Accelerated Review)

9411-093

(T/V/C/Melanoma)

Dranoff, Glen; Dana Farber Cancer Institute, Boston, Massachusetts; *A Phase I Study of Vaccination with Autologous, Irradiated Melanoma Cells Engineered to Secrete Human Granulocyte-Macrophage Colony Stimulating Factor.*  
NIH/ORDA Approval: 11-23-94 (Accelerated Review)

9412-094

(T/IGD/CF)

Dorkin, Henry L.; New England Medical Center, Tufts University, Boston, Massachusetts; and Lapey, Allen; Massachusetts General Hospital, Harvard Medical School, Boston, Massachusetts; *Adenovirus Mediated Gene Transfer for Cystic Fibrosis: Safety of a Single Administration in the Lung (aerosol administration).*  
RAC Approval: 12-1-94/NIH Approval: Pending

9412-095

(T/C/Solid Malignant Tumors or Lymphomas)

Hersh, Evan; Akporiaye, Emmanuel; Harris, David; Stopeck, Alison; Unger, Evan; and Warneke, James; Arizona Cancer Center, Tucson, Arizona; *Phase I Trial of Interleukin-2 Plasmid DNA/DMRIE/DOPE Lipid Complex as an Immunotherapeutic Agent in Solid Malignant Tumors or Lymphomas by Direct Gene Transfer.*  
RAC Approval: 12-1-94/NIH Approval: Pending

9412-096

(T/C/Head and Neck Squamous Cell Carcinoma)

Clayman, Gary; MD Anderson Cancer Center, Houston, Texas; *Clinical Protocol for Modification of Tumor Suppressor Gene Expression in Head and Neck Squamous Cell Carcinoma (HNSCC) with an Adenovirus Vector Expressing Wild-type p53.*  
RAC Approval: 12-2-94/NIH Approval: Pending

9412-097

(T/C/Primary and Metastatic Liver Tumors)

Venook, Alan and Warren, Robert; University of California, San Francisco, California; *Gene Therapy of Primary and Metastatic Malignant Tumors of the Liver Using ACN53 Via Hepatic Artery Infusion: A Phase I Study.*  
RAC Approval: 12-2-94/NIH Approval: Pending

9412-098

(T/C/Central Nervous System Malignancies)

Grossman, Robert and Woo, Savio; Baylor College of Medicine, Houston, Texas; *Phase I Study of Adenoviral Vector Delivery of the HSV-TK Gene and the Intravenous Administration of Ganciclovir in Adults with Malignant Tumor of the Central Nervous System.*  
RAC Approval: 12-2-94/NIH Approval: Pending

9502-099

(T/C/Malignant Glioma)

Fetell, Michael; Columbia Presbyterian Medical Center, New York, New York; *Stereotaxic Injection of Herpes Simplex Thymidine Kinase Vector Producer Cells (PA317/GITkSvNa.7) and Intravenous Ganciclovir for the Treatment of Recurrent Malignant Glioma.*  
NIH/ORDA Approval: 2-10-95 (Accelerated Review)

	T	M	Total (T + M)
<b>RAC APPROVED</b> (including Accelerated Review)	74	25	99
<b>NIH APPROVED</b>	64	25	89

**LEGEND:**

- a** = Minor Modification(s)
- b** = Major Amendment(s)
- = RAC Approved/NIH Approval Pending

**ACRONYMS:**

BM	Autologous Bone Marrow Cells
BM/PB	Autologous Bone Marrow and Peripheral Blood Cells
BMSC	Autologous Bone Marrow Stem Cells
C	Cancer
CTL	Autologous Cytotoxic T Lymphocytes
EBV-CTL	Epstein-Barr Virus Specific Cytotoxic T Cell Lines
H	Autologous Hepatocytes
HIV	Human Immunodeficiency Virus
IGD	Inherited Genetic Disorder
M	Gene Marking Protocol
O	Other
PB	Autologous Peripheral Blood Cells
PBSC	Autologous Peripheral Blood Stem Cells
SCID-ADA	Severe Combined Immunodeficiency Due to Adenosine Deaminase Deficiency
T	Gene Therapy Protocol
TIL	Autologous Tumor Infiltrating Lymphocytes
V	Vaccine (Lethally Irradiated Cells)

February 24, 1995

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